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| 10/535,581 | 01/17/2006 | Thomas Link | 23062 | 7537 |

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| EXAMINER | |
|---|---|
| BARNHART, LORA ELIZABETH | |
| ART UNIT | PAPER NUMBER |
| 1651 | |

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/535,581 | LINK ET AL. | |
| | Examiner | Art Unit | |
| | Lora E. Barnhart | 1651 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *09 February 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *16-20 and 22-27* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/10/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

As discussed in the previous Office action, applicant is requested to specifically point out the support for any amendments made to the disclosure in response to this Office action, including the claims (MPEP 714.02 and 2163.06). In doing so, applicant is requested to refer to pages and line numbers in the as-filed specification, **not** the published application. The reply makes reference to various paragraph numbers that do not correlate to the as-filed specification, which has no paragraph numbers.

### *Response to Amendments*

Applicant's amendments filed 12/10/08 and 2/9/09 to claims 16, 23, and 25 have been entered. Claim 21 has been cancelled. No claims have been added. Claims 16-20 and 22-27 remain pending in the current application, all of which are being considered on their merits. References not included with this Office action can be found in a prior action. Any rejections of record not particularly addressed below are withdrawn in light of the claim amendments and applicant's comments.

### *Election/Restrictions*

Applicant's election with traverse of the species "CHO cells" and "immunoglobulins" in the reply filed on 5/13/08 is still in effect over the claims.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16-20 and 22-27 are also rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The courts have described the essential question to be addressed in a description requirement issue in a variety of ways. An objective standard for determining compliance with the written description requirement is, "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989). Under *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991), to satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, and that the invention, in that context, is whatever is now claimed. The test for sufficiency of support in a parent application is whether the disclosure of the application relied upon "reasonably conveys to the artisan that the inventor had possession at that time of the later claimed subject matter." *Ralston Purina Co. v. Far-Mar-Co.*, Inc., 772 F.2d 1570, 1575, 227 USPQ 177, 179 (Fed. Cir. 1985) (quoting *In re Kaslow*, 707 F.2d 1366, 1375, 217 USPQ 1089, 1096 (Fed. Cir. 1983)). Whenever the issue arises, the fundamental factual inquiry is whether the specification conveys with reasonable clarity to those

skilled in the art that, as of the filing date sought, applicant was in possession of the invention as now claimed. See, e.g., *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). See M.P.E.P. § 2163.02.

In this case, the skilled artisan would not have reasonably concluded at the time of the invention that applicant was in possession of the entire invention as claimed because the media required to carry out the claimed method is not adequately described in the specification.

The claims are drawn to a method of producing an immunoglobulin by culturing CHO cells that produce that immunoglobulin in a media that provides a desired degree of glucose limitation (DGL). However, the specification provides insufficient description of the media that the skilled artisan would immediately envisage the components that comprise the media.

In the instant application, **no media or culture conditions suitable for practicing the method are particularly disclosed and described.** At page 7, the disclosure speculates, "In principle[,] any glucose-containing medium can be used as the culture medium which is not limiting in regard to other components." The working examples are limited to a few in which two specific proteins (MUC-Ig2a fusion protein and "MUC-C-term," presumably a truncation mutant of MUC) are produced from CHO cells that appear to have been engineered specifically for the production of these fusion proteins. However, the contents of the media are not clearly indicated in the specification, and the manner in which glucose is included such that the requirements of the claim are met is not clear.

The specification does not define any of the media used in the methods by listing components and their concentrations therein. No method is provided for identifying components having the function necessary to carry out the method (other than implied trial-and-error), and no component is particularly described. For this reason, the rejection due to lack of written description is proper.

Applicant alleges that the specification indicates that any medium containing glucose may be used and that identifying the appropriate conditions would have required only routine optimization (Reply, page 6; and page 7, last paragraph). Applicants allege that "specific examples of the cultivation media are given" in the specification (Reply, page 7, paragraph 1). These arguments have been fully considered, but they are not persuasive.

Applicant's statement that the specification includes "specific examples" of the cultivation media is not supported by reference to any page of the specification. Prosecution would be aided by a clear indication of which pages of the as-filed specification (**not** the published application) provide these "specific examples." At page 3, paragraph 1, the specification requires that there be "no other limitation by other substrates before the onset of glucose limitation," but no examples of media are provided that are completely non-limiting for each and every substrate for each and every substrate for each and every possible process in the culture process.

Applicant's comments generally allege that any media containing glucose could be used to practice this invention, which appears to be an admission that the instantly claimed method is obvious, especially since the claim limitations do

not require that any particular amount of glucose is present or that any particular culturing step is required (see rejections under 35 U.S.C. § 112, second paragraph). At this time, the examiner chooses not to interpret the comments at page 6 as being an admission of obviousness.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-20 and 22-27 remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 16 requires culturing cells in "a nutrient media that results in a degree of glucose limitation (DGL)," wherein the DGL is further defined in terms of a ratio and in terms of its relationship to a minimum level. These limitations do not particularly define the media by its structural and physical properties, but rather wholly by its function, which is improper. See *In re Schreiber*, 128 F.3d 1473, 1477-78, 44 USPQ2d 1429, 1431-32 (Fed. Cir. 1997). The claim does not particularly point out what components are necessarily included and excluded from the media. Clarification is required.

Claim 16 refers to "the DGL needed for maintenance of the cell," but this term is not clear. First, the nature of the "maintenance" is not pointed out; it is not clear whether the cell must simply survive or whether it must produce the substance of interest. Second, it is not clear how this value would be determined for any given cell. Clarification is required.

Claim 16 requires that the media's composition depend on two variable elements, which renders the claim indefinite. In the media of claim 16, the DGL ratio between the "**currently** observed specific glucose consumption rate" and the "maximum **known** specific glucose consumption rate" must be equal to or below 0.5, but the terms "currently observed" and "maximum known" do not place any particular limits on these rates. There is no basis provided for the comparative term "currently," and the claim indicates by use of the term "maximum known rate" that the scope may change depending on some unknown future findings of skilled artisans. There is no guidance for identifying these numbers for a given cell under given conditions. Clarification is required.

In short, the claims place no particular limits on the components of the media; the media is described wholly in functional terms. **The claims are currently so indefinite that they cannot be meaningfully examined.** The claims should particularly point out the physical and structural characteristics of the media that is used in the method. Because claims 17-20 and 22-27 depend from indefinite claim 16 and do not clarify these points of confusion, they must also be rejected under 35 U.S.C. 112, second paragraph.

Regarding these rejections, applicants allege, "the only parameter to be known is the specific glucose consumption rate of the cultivated CHO cell" (Reply, page 8, last paragraph), but again, this rate is not defined in the claims, has not been provided with a limiting definition in the specification, and has not been established on the record as being an term of art.

Applicants allege that “maintenance” is defined in the specification, but it is respectfully submitted that applicants are selectively quoting from the disclosure. The entire sentence referenced by applicants at page 9, paragraph 1, of the reply, reads: "The method according to the invention reduces the amount of glucose that is available per cell in such a manner that glucose is mainly used in maintenance metabolism and thus for the product and less for cell growth." With all due respect, this sentence does not appear to constitute a clear, limiting definition of “maintenance.”

Applicants allege that the glucose consumption rate of CHO cells “will not be changed due to future findings,” but this statement is unsubstantiated by declarations of skilled artisans or citations of prior art. The amendments to the claims do not address the question of the basis of comparison for the relative term "currently.” It is submitted that “currently observed” does not necessarily refer to observations during any particular time point in the method or otherwise.

Claims 19 and 20 refer to the “maximum **expected** cell count,” which is confusing. It is not clear who or what is expecting the cells to be present in a particular number. Furthermore, this term places no particular limit on the number. It is simply not clear what variable applicant means to reference. Clarification is required.

Applicant replies to this rejection with an essentially tautological statement that the maximum expected cell count is the maximum density that can be obtained. The examples in the specification are just that: examples. The

specification does not indicate under which particular conditions this "maximum" density was obtained, and the claims do not require that the conditions for which the maximum count is determined are the same as those under which the claimed method is carried out.

Claims 19 and 20 also refer to an amount of glucose to be consumed by the cells, but this amount is defined entirely in functional terms. It is not clear what amount is required or how the amount would even be measured. Clarification is required.

Applicant alleges that the amount of glucose cannot be specified in absolute terms, which appears to constitute acquiescence to the rejection. Again, the key issue with these claim limitations is that they are functional and describe the media by what it does, rather than what it is.

Claim 22 does not appear to further limit claim 16, since claim 16 limits the product to "immunoglobulins" and claim 22 broadens the scope of the product to "proteins or polypeptides." Similarly, claim 23 appears to broaden the scope of claim 16, rather than limit it. Clarification is required.

Claim 24 refers to "before glucose limitation occurs," which is confusing. It is not clear how this claim relates to the independent claim temporally. Clarification is required.

Applicant alleges that this limitation refers to “the beginning of the cultivation,” but it is submitted that the claims make no such requirement.

Claim 25 requires that the glucose be fed “separately,” but the point of comparison for this relative term is not pointed out. Clarification is required.

Claims 16-20 and 22-27 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention. Evidence that the claims fail to correspond in scope with that which applicant(s) regard as the invention can be found in the reply filed 2/9/09. In that paper, applicant has stated that the media cannot be limiting for any substrate other than glucose (Reply, page 5, paragraph 2, e.g.), and this statement indicates that the invention is different from what is defined in the claim(s) because the claims are silent as to any limitation other than glucose limitation. Furthermore, the comments refer to "the inventive step of measuring DGL in the cultivation medium” (Reply, page 7, paragraph 1), but the claims include no such measuring step.

***No claims are allowed.***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lora E. Barnhart whose telephone number is (571)272-1928. The examiner can normally be reached on Monday-Thursday, 9:00am - 5:30pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Lora E Barnhart/
Primary Examiner, Art Unit 1651